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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/986,234	10/22/2001	Mitchell A. Lazar	053893-5032-01	4995

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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 01/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/986,234	LAZAR, MITCHELL A.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10,11,23,24 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,11,23,24 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 10, 11, 23, 24, and 34 are being acted upon.

2. Applicant's amendments and remarks filed 11/03/05, are acknowledged. In view of the amendments, all previous rejections have been withdrawn.

3. The following are new grounds for rejection.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 10, 11, 23, 24, and 34 are rejected under 35 U.S.C. 112, first paragraph, because the specification,
while being enabling for,
a method of treating or alleviating type II diabetes comprising administering to a mouse afflicted with type II diabetes a composition comprising an antibody that binds the resistin encoded by SEQ ID NO:2 or SEQ ID NO:4 in an amount sufficient to reduce serum glucose,
does not reasonably provide enablement for,
a method of treating or alleviating type II diabetes comprising administering to a patient (other than a mouse) afflicted with type II diabetes a composition comprising an antibody that binds the resistin encoded by SEQ ID NO:2 or SEQ ID NO:4 in an amount sufficient to reduce serum glucose.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

With regards to the instant claims, the level of predictability of the art (particularly in view of the state of the prior art), the amount of direction provided by the inventor, and the existence of working examples (or lack thereof), comprise the major factors to be considered. Early work with resistin showed that in rodent models upregulation of the polypeptide (SQ ID NO:2) correlated with insulin resistance and high serum glucose levels, and that a reduction of serum resistin resulted in a reduction of serum glucose levels. Accordingly, it might have been presumed that a human homologue (SEQ ID NO:4) would have a similar activity in humans. Numerous studies, however, have shown that resistin levels in humans do not correlate with insulin resistance, and thus, serum glucose levels. Note that this finding was not completely unexpected given that human and mouse resistin are just 56% identical, their gene organization is highly diverse, and the polypeptides are expressed in different tissues. Accordingly, the art shows that a method of treating or alleviating type 2 diabetes in humans, by reducing serum glucose, comprising reducing resistin levels, must be considered to be unpredictable and requiring of undue experimentation.

See, for example, Lee et al. (2003). The authors found no significant difference in resistin levels between obese nondiabetic and obese type 2 diabetic subjects (see particularly page 4852, column 2). The authors conclude, "We present one of

the first human studies on circulating resistin levels and, using a highly specific ELISA, find no evidence supporting a role for serum resistin in mediating insulin resistance or reflecting obesity in humans" (page 4853, **Discussion**). Other investigators have come to similar conclusions. See, for example, Heilbronn et al. (2004), "Our study did not demonstrate an independent association between resistin and insulin sensitivity. Furthermore, although resistin was up-regulated by insulin, this effect was modest and was not observed in all subjects. Although the exact function of resistin remains unclear, this study does not support a role for resistin as a major mediator of insulin sensitivity in humans" (page 1847, **Conclusion**). In a study of Pima Indians, a population with a high prevalence of type 2 diabetes, Volarova de Courten et al. (2004) found that "high serum resistin levels were cross-sectionally associated with adiposity, but not with whole-body or hepatic insulin resistance" (page 1282, **Discussion**). As at least regards insulin resistance, even newer work continues with the same findings, see, for example, Iqbal et al. (2005), "**Serum resistin is not associated with obesity or insulin resistance in humans**" (title).

In view of the findings set forth above, the instant specification would require a significant amount of guidance to enable the claimed method. A review of the specification, however, reveals no significant guidance and no working examples of a method of treating or alleviating type 2 diabetes in humans, by reducing serum glucose, comprising reducing resistin levels. All of the examples set forth in the disclosure employ rodent models. Given that the art teaches that in this instance the results in animal models do not accurately reflect results likely to be achieved in humans, the method of the instant claims must be considered to be unpredictable and requiring of undue experimentation.

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

8. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

1/14/07

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